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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Milind Rajopadhye, et al.

Confirmation No.: 7274

Application No.: 09/281,474

Group Art Unit: 1618

Filing Date: March 30, 1999

Examiner: Dameron Levest Jones

For: PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS

EXPRESS MAIL LABEL NO: EV 765643723 US
DATE OF DEPOSIT: January 25, 2006

EV765643723US

MS Appeal Brief - Patent
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**APPEAL BRIEF TRANSMITTAL
PURSUANT TO 37 CFR § 1.192**

Transmitted herewith in triplicate is the APPEAL BRIEF in this application with respect to the Notice of Appeal received by The United States Patent and Trademark Office on **August 25, 2005**.

- Applicant(s) has previously claimed small entity status under 37 CFR § 1.27 .
- Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR § 1.27 as:
 - an Independent Inventor
 - a Small Business Concern
 - a Nonprofit Organization.
- Petition is hereby made under 37 CFR § 1.136(a) (fees: 37 CFR § 1.17(a)(1)-(4)) to extend the time for response to the Notice of Appeal received by the United States Patent and Trademark Office on August 25, 2005 to and through January 25, 2006 comprising an extension of the shortened statutory period of 3 month(s).

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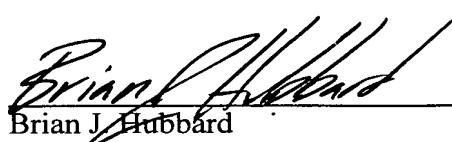
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	SMALL ENTITY		NOT SMALL ENTITY	
	RATE	Fee	RATE	Fee
<input checked="" type="checkbox"/> APPEAL BRIEF FEE	\$250	\$	\$500	\$500
<input type="checkbox"/> ONE MONTH EXTENSION OF TIME	\$60	\$	\$120	\$----
<input type="checkbox"/> TWO MONTH EXTENSION OF TIME	\$225	\$	\$450	\$----
<input checked="" type="checkbox"/> THREE MONTH EXTENSION OF TIME	\$510	\$	\$1020	\$1020
<input type="checkbox"/> FOUR MONTH EXTENSION OF TIME	\$795	\$	\$1590	\$----
<input type="checkbox"/> FIVE MONTH EXTENSION OF TIME	\$1080	\$	\$2160	\$----
<input type="checkbox"/> LESS ANY EXTENSION FEE ALREADY PAID	minus	(\$)	minus	(\$----)
TOTAL FEE DUE		\$0		\$1520

- The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is further authorized to charge any fees related to any such extension of time to Deposit Account 23-3050. This sheet is provided in duplicate.
- A check in the amount of \$1,520.00 is attached. Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050.
- Please charge Deposit Account No. 23-3050 in the amount of \$ ____ .00. This sheet is attached in duplicate.
- The Commissioner is hereby authorized to charge any deficiency or credit any overpayment of the fees associated with this communication to Deposit Account No. 23-3050.

Date: Jan. 25, 2006



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PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: **Milind Rajopadhye et al.** Confirmation No.: **7274**

Serial No.: **09/281,474**

Group Art Unit: **1618**

Filing Date: **March 30, 1999**

Examiner: **Dameron L. Jones**

For: **Pharmaceuticals For The Imaging Of Angiogenic Disorders**

EXPRESS MAIL LABEL NO: EV 765643723 US

DATE OF DEPOSIT: January 25, 2006

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

This Brief is being filed in support of Appellant's appeal from the rejections of claims 1-10, 12-35, 48-50, 52 and 53 dated May 25, 2005. A Notice of Appeal was filed on August 25, 2005.

1. REAL PARTY IN INTEREST

Bristol-Myers Squibb Company by virtue of the assignment recorded December 3, 2002, at Reel 012607 Frame 0038.

500.00 IP

2. RELATED APPEALS AND INTERFERENCES

None.

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3. STATUS OF CLAIMS

Claim 1	Rejected and On Appeal	Claim 28	Rejected and On Appeal
Claim 2	Rejected and On Appeal	Claim 29	Rejected and On Appeal
Claim 3	Rejected and On Appeal	Claim 30	Rejected and On Appeal
Claim 4	Rejected and On Appeal	Claim 31	Rejected and On Appeal
Claim 5	Rejected and On Appeal	Claim 32	Rejected and On Appeal
Claim 6	Rejected and On Appeal	Claim 33	Rejected and On Appeal
Claim 7	Rejected and On Appeal	Claim 34	Rejected and On Appeal
Claim 8	Rejected and On Appeal	Claim 35	Rejected and On Appeal
Claim 9	Rejected and On Appeal	Claim 36	Canceled
Claim 10	Rejected and On Appeal	Claim 37	Canceled
Claim 11	Canceled	Claim 38	Canceled
Claim 12	Rejected and On Appeal	Claim 39	Canceled
Claim 13	Rejected and On Appeal	Claim 40	Canceled
Claim 14	Rejected and On Appeal	Claim 41	Canceled
Claim 15	Rejected and On Appeal	Claim 42	Canceled
Claim 16	Rejected and On Appeal	Claim 43	Canceled
Claim 17	Rejected and On Appeal	Claim 44	Canceled
Claim 18	Rejected and On Appeal	Claim 45	Canceled
Claim 19	Rejected and On Appeal	Claim 46	Canceled
Claim 20	Rejected and On Appeal	Claim 47	Canceled
Claim 21	Rejected and On Appeal	Claim 48	Rejected and On Appeal
Claim 22	Rejected and On Appeal	Claim 49	Rejected and On Appeal
Claim 23	Rejected and On Appeal	Claim 50	Rejected and On Appeal
Claim 24	Rejected and On Appeal	Claim 51	Canceled
Claim 25	Rejected and On Appeal	Claim 52	Rejected and On Appeal
Claim 26	Rejected and On Appeal	Claim 53	Rejected and On Appeal
Claim 27	Rejected and On Appeal		

4. STATUS OF AMENDMENTS

The claims have not changed since the response of February 18, 2005.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The "present invention provides a novel compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator." *Appellants' Detailed Description*, corresponding to para. [0025] of the published application US 2002/0001566. Note that it is a single compound that has two distinct parts, one part being a peptide or peptidomimetic targeting moiety (which binds to a receptor that is upregulated during angiogenesis), and the other part being a chelator. In operation, the compound can target areas of increased angiogenesis, the targeting moiety providing specificity, and the attached chelator providing a selected metal for diagnosis or therapy.

Appellants have three independent claims of varying scope. The broadest, Independent Claim 52 recites "[a] compound comprising a peptide or peptidomimetic α,β_3 receptor targeting moiety bound to a chelator." Independent Claim 1 includes a linking group defined by structure between the targeting moiety and chelator, reciting "[a] compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis, the receptor is α,β_3 , and the compound has a linking group between the targeting moiety and chelator, the linking group having the formula: $(CR^6R^7)_g-(W)_h-(CR^{6a}R^{7a})_g-(Z)_k-(W)_h-(CR^{8a}R^{9a})_g \dots$ ". Independent Claim 53 recites a list of chelators by name, reciting "[a] compound, comprising a peptide or peptidomimetic α,β_3 receptor targeting moiety bound to a chelator, wherein said chelator is a diaminedithiol, monoamine-monoamidedithiol, triamide-monothiol, monoamine-diamide-monothiol,

diaminedioxime, hydrazine, or cyclic polyaminocarboxylate, or acyclic polyaminocarboxylate."

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the Examiner has demonstrated that Claims 1, 2, 12-15, 17, 19-21, 25, 27, 28, 31-35, 48-50, 52 and 53 are unpatentable under 35 U.S.C. §103(a) over US Patent No 5,780,426 (hereinafter the Palladino reference) in view of US Patent No. 6,331,285 (hereinafter the Sharma reference).

Whether the Examiner has demonstrated that Claims 1-10, 12-35, 48-50, 52, and 53 are provisionally unpatentable under the judicially created doctrine of obviousness-type double patenting against copending applications Serial Nos. 09/465,300 (now U.S. Patent 6,511,648), 09/466,582 (now U.S. Patent 6,558,649), 09/599,364 (now U.S. Patent 6,511,649), 09/281,209 (now U.S. Patent 6,524,553), and 09/948,807 (now U.S. Patent 6,683,163).

7. ARGUMENT

I. Whether the Examiner has demonstrated that Claims 1, 2, 12-15, 17, 19-21, 25, 27, 28, 31-35, 48-50, 52 and 53 are unpatentable under 35 U.S.C. §103(a) over the Palladino reference in view of the Sharma reference.

A. Claim 52¹

1. The Combination Of Reference Fails To Meet All Claim Limitations

Independent claim 52 recites "[a] compound comprising a peptide or peptidomimetic

¹ To minimize repetition of arguments, Appellants are treating the claims in the following order: Claim 52, Claim 1, Claims 2, 12-15, 17, 19-21, 25, 27, 28, 31-35, 48-50, and Claim 53.

$\alpha_v\beta_3$ receptor targeting moiety bound to a chelator." (emphasis added).

The Palladino reference discloses "non-RGD cyclic peptides that inhibit the function of the integrin receptor, $\alpha_v\beta_3$." *Id.* at Abstract. These peptides target and bind the receptor, thereby acting therapeutically. *Id.* at col. 7, lines 20-25.

However, the Palladino reference lacks a chelator, or in the alternative, lacks the limitation of the "targeting moiety **bound to a chelator**." The Examiner seems to agree, as the Sharma reference is applied as the secondary reference, but the Examiner does discuss labels in the Palladino reference, citing col. 6, lines 37-55 (lines 37-40 of which state "As used herein, the terms 'label' or 'labeled' refers to incorporation of a detectable marker, e.g., by incorporation of a radiolabeled amino acid or attachment to a polypeptide of biotinyl moieties that can be detected by marked avidin" (emphasis added)) and the bridging paragraph of col. 20-21.

The Palladino reference is specifically concerned with detecting formation of an antibody complex involving the peptides. *Id.* at col. 20, lines 56-57. Taking the paragraphs before and after the bridging paragraph puts the disclosure into better context and makes it clear that the reference is referring to immunological labeling techniques as opposed to chelators:

The word "complex" as used herein refers to the **product of a specific binding reaction such as an antibody-antigen or receptor-ligand reaction**. Exemplary complexes are **immunoreaction products**.

As used herein, the terms "label" and "indicating means" in their various grammatical forms refer to single atoms and molecules that are either directly or indirectly involved in the production of a detectable signal **to indicate the presence of a complex**. "In Vivo" labels or indicating means are those useful within the body of a human subject and include .sup.111 In, .sup.99 Tc, .sup.G.alpha., 186 Re, and .sup.32 I. Any label or indicating means can be linked to or incorporated in an expressed protein, polypeptide, or antibody molecule **that is part of an antibody or monoclonal antibody composition of the present invention**, or used separately, and those atoms or molecules can be used alone or in conjunction with additional reagents. Such labels are

themselves well-known in clinical diagnostic chemistry and constitute a part of this invention only insofar as they are utilized with otherwise novel protein methods and/or systems.

The linking of labels, i.e., labeling of, polypeptides and proteins is well known in the art. For instance, **antibody molecules produced by a hybridoma can be labeled** by metabolic incorporation of radioisotope-containing amino acids provided as a component in the culture medium. See, for example, Galfre et al., Meth. Enzymol., 73: 3-46 (1981). The techniques of **protein conjugation** or coupling through activated functional groups are particularly applicable. See, for example, Aurameas, et al., Scand. J. Immunol., 8 Suppl. 7: 7-23 (1978); Rodwell et al., Biotech., 3: 889-894 (1984) and U.S. Pat. No. 4,493,795.

col. 20, line 60 to col. 21, line 12 (emphasis added). No chelators appear to be disclosed.

Additionally, neither a radiolabeled amino acid nor a labeled complex (where it is just as likely that the antibody is labeled) meets the claim limitation of a "targeting moiety **bound to a chelator.**"

The Sharma reference relates to conformationally fixed peptides and metallo-constructs that have a metal ion binding backbone *Id.* at col. 1, *Field of Invention*. A metal is attached to O, N, or S, atoms present in the backbone or side chains of the peptide. Thus, Sharma also fails to teach a "targeting moiety **bound to**" a chelator. The Examiner refers to col. 37, lines 35-45 and col. 39, lines 50-60. Appellants submit that both merely show a peptide coordinating a metal, which bolsters Appellants point. In fact, in col. 39, the Sharma reference states "[i]n these constructs a metal binding site is introduced **between** two pre-selected ends of a linear peptide that contains the biological function domain." *Id.* at col. 39, lines 45-48 (emphasis added). If the peptide targeting moiety *is* the chelator, it's not "bound to" the chelator.

Therefore, even when combined, the references fail to teach all limitations of the claims. As such, the rejection was improper.

2. The References Lack Motivation To Be Properly Combined

Appellants question the motivation to combine the Palladino reference and the Sharma reference. Both concern targeting the integrin receptor, but their mechanisms appear quite different. The Palladino reference has a **non-RGD** targeting moiety that does not appear to be conformationally fixed. In contrast, the Sharma reference has a **conformationally fixed RGD** containing peptide.

Appellants do not believe that the Examiner has ever addressed what modifications would have to take place, *i.e.*, what features of each reference would be retained and how they would interrelate. If one skilled in the art removed the "conformationally fixed" portion of the Sharma reference, the metal binding ability would be lost, thus, there is no motivation. On the other hand, the Examiner has cited no evidence that the Palladino reference's **non-RGD** targeting moiety could be conformationally fixed and retain activity. If it causes the targeting moiety to lose activity, the modification would be unsatisfactory for its intended purpose. *See* MPEP 2143.01.

B. Claim 1

Claim 1 recites "[a] compound, comprising: a targeting moiety and a chelator, wherein the **targeting moiety is bound to the chelator**, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis, the receptor is $\alpha_1\beta_3$, and the compound has a linking group between the targeting moiety and chelator, **the linking group having the formula:** $(CR^6R^7)_g-(W)_h-(CR^{6a}R^{7a})_g'-(Z)_k-(W)_l'-(CR^8R^9)_g''-(W)_h'''-(CR^{8a}R^{9a})_g''' \dots$ ". (emphasis added).

The Examiner has failed to provide a *prima facie* case of obviousness for the reasons discussed with respect to claim 52, *above*. The rejection is additionally defective for the following.

Claim 1 recites a linking group with a specified structure. The Palladino reference states that "[i]n some embodiments, labels are attached by spacer arms of various lengths to reduce potential stearic hindrance." *Id.* at col. 6, lines 54-55. However, the labels are not chelators, and thus the limitation of "a linking group between the targeting moiety and chelator" cannot be met. The Examiner also failed to analyze how one skilled in the art, armed with the Palladino reference's single disclosure of "spacer arms" (found solely at col. 6, lines 54-55) would arrive at Appellants claimed formula.

The Examiner cites the Sharma reference as having spacer sequences that presumably she considers a linking group. The Sharma reference states:

The **metal ion-binding backbone** may also include a derivatized amino acid or spacer sequence, wherein the derivatized amino acid or spacer sequence includes at least one **nitrogen, sulfur or oxygen atom** available for complexing with the available valences of the metal ion, so that all of the valences of the metal ion are satisfied upon complexation of the metal ion.

Id. at col. 10, lines 39-45 (emphasis added).

Appellants submit that if the spacer sequence is "complexing with the available valences of the metal ion" it would be the chelator, not a linking group. Moreover, by being incorporated into the peptide backbone, the spacer sequence is not "a linking group **between** the targeting moiety and chelator."

Additionally, the Examiner has made no finding that the examples of spacer sequences that were referenced (col. 28, lines 23-45) even conform to Appellants claimed formula, which improperly fails to consider and give weight to all claim limitations.

Thus, the Examiner failed to provide a *prima facie* case of obviousness for Claim 1.

C. Claims 2, 12-15, 17, 19-21, 25, 27, 28, 31-35, and 48-50

These claims depend from and further limit claim 1, and thus patentably define over the art of record for the same reasons.

D. Claim 53

Claim 53 recites "[a] compound, comprising a peptide or peptidomimetic $\alpha\beta$ receptor targeting moiety bound to a chelator, **wherein said chelator is a diaminedithiol, monoamine-monoamidedithiol, triamide-monothiol, monoamine-diamide-monothiol, diaminedioxime, hydrazine, or cyclic polyaminocarboxylate, or acyclic polyaminocarboxylate.**" (emphasis added).

The Examiner has failed to provide a *prima facie* case of obviousness for the reasons discussed with respect to claim 52, *above*. Basically, when required to supply a "chelator" to make a *prima facie* showing, the Examiner has presented biologically active peptides which have a metal ion-binding backbone (the Sharma reference), and thus no separate chelator portion to be "bound to." In claim 53, the Examiner apparently relies on the peptide backbone to render obvious Appellants specific list of chelators.

The MPEP requires that all claim limitations must be taught or suggested. MPEP §2143.03. Appellants are fairly certain that the Examiner has not addressed how the claim limitation "**wherein said chelator is a diaminedithiol, monoamine-monoamidedithiol, triamide-monothiol, monoamine-diamide-monothiol, diaminedioxime, hydrazine, or cyclic polyaminocarboxylate, or acyclic polyaminocarboxylate**" is rendered obvious by the references, either singly or in combination. This is improper as the Examiner has not met her burden. *See* MPEP §2142 ("either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the

artisan would have found the claimed invention to have been obvious in light of the teachings of the references").

II. Whether the Examiner has demonstrated that claims 1-10, 12-35, 48-50, 52, and 53 are unpatentable under the provisional double patenting rejections based on the judicially created doctrine of obviousness-type double patenting against copending applications Serial Nos. 09/465,300 (now U.S. Patent 6,511,648), 09/466,582 (now U.S. Patent 6,558,649), 09/599,364 (now U.S. Patent 6,511,649), 09/281,209 (now U.S. Patent 6,524,553), and 09/948,807 (now U.S. Patent 6,683,163).

Claims 1-10, 12-35, 48-50, and 52, and 53

1. Serial No. 09/465,300 (now U.S. Patent 6,511,648)

The '648 patent relates to a compound, comprising a targeting moiety and a chelator, wherein the targeting moiety is a quinolone nonpeptide. In contrast, the Appellants claims recite that the targeting moiety is a "peptide or peptidomimetic." Thus, the disclosures *teach away* from each other. MPEP §804 states that:

... the factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. ... Any obviousness-type double patenting rejection should make clear: (A) **The differences between the inventions defined by the conflicting claims** — a claim in the patent compared to a claim in the application; and (B) **The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.** When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art.

(emphasis added). The Examiner failed to establish a *prima facie* case of obviousness-type double patenting and the rejection is improper.

2. Serial No. 09/466,582 (now U.S. Patent 6,558,649)

The '649 patent relates to a compound, comprising a targeting moiety and a chelator, wherein the targeting moiety is a benzodiazepine nonpeptide. In contrast, the Appellants claims recite that the targeting moiety is a "peptide or peptidomimetic." Thus, the disclosures *teach away* from each other. The Examiner failed to establish a *prima facie* case of obviousness-type double patenting and the rejection is improper.

3. Serial No. 09/599,364 (now U.S. Patent 6,511,649)

The '649 patent relates to a compound, comprising a targeting moiety and a chelator, wherein the targeting moiety is a quinolone non-peptide. In contrast, the Appellants claims recite that the targeting moiety is a "peptide or peptidomimetic." Thus, the disclosures *teach away* from each other. Moreover, the '649 patent includes "at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent," which further differentiates the inventions. The Examiner failed to establish a *prima facie* case of obviousness-type double patenting and the rejection is improper.

4. Serial No. 09/281,209 (now U.S. Patent 6,524,553)

The '553 patent relates to a compound, comprising a targeting moiety and a chelator, wherein the targeting moiety is a nonpeptide. In contrast, the Appellants claims recite that the targeting moiety is a "peptide or peptidomimetic." Thus, the disclosures *teach away* from each other. Moreover, the '553 patent claims a surfactant bound to the targeting moiety, not a

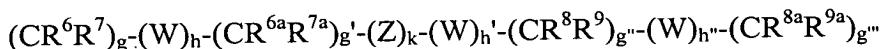
chelator. The Examiner failed to establish a *prima facie* case of obviousness-type double patenting and the rejection is improper.

5. Serial No. 09/948,807 (now U.S. Patent 6,683,163)

The '163 patent claims 4 specific structures. The structures show a quinolone nonpeptide portion. The detailed description (col. 6, lines 45-46) states that the targeting moiety is a quinolone nonpeptide. In contrast, the Appellants claims recite that the targeting moiety is a "peptide or peptidomimetic." Thus, the disclosures *teach away* from each other. The Examiner failed to establish a *prima facie* case of obviousness-type double patenting and the rejection is improper.

8. CLAIMS APPENDIX

1. (Rejected and On Appeal) A compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis, the receptor is $\alpha_v\beta_3$, and the compound has a linking group between the targeting moiety and chelator, the linking group having the formula:



wherein,

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ and R^{9a} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁-C₅ alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁-C₅ alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to the chelator;

R¹⁰ is independently selected at each occurrence from the group: a bond to the chelator, COOR¹¹, OH, NHR¹¹, SO₃H, PO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered

heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 01 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, and a bond to the chelator;

R¹² is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h" is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

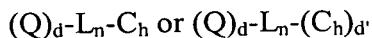
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; and

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

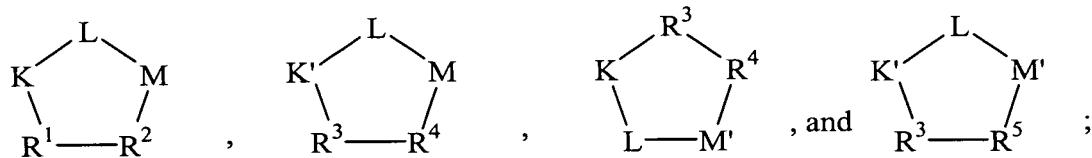
with the proviso that at least one of k, h, h', h'', g, g', g'', and g''' is other than 0.

2. (Rejected and On Appeal) A compound according to Claim 1, wherein the targeting moiety is a peptide or a mimetic thereof and the linking group is present between the targeting moiety and chelator.

3. (Rejected and On Appeal) A compound according to Claim 2, the compound is of the formula:



wherein, Q is a peptide independently selected from the group:



K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylornithine, δ -N-benzylcarbamoylornithine, and β -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a-D amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylornithine, δ -N-benzylcarbamoylornithine, and β -2-benzimidazolylacetyl-1, 2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;

R¹ is an amino acid substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;

R² is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, methionine, and 2-aminothiazole-4-acetic acid;

R³ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, and D-methionine;

R⁴ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-

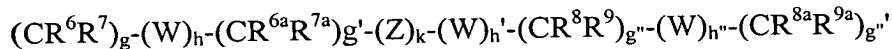
phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, D-methionine, and 2-aminothiazole-4-acetic acid;

R^5 is an amino acid, substituted with 0-1 bonds to L_n , independently selected at each occurrence from the group: glycine, L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-serine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine, L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of R^1 , R^2 , R^3 , R^4 , and R^5 in each Q is substituted with a bond to L_n , further provided that when R^2 is 2-aminothiazole-4-acetic acid, K is N-methylarginine, further provided that when R^4 is 2-aminothiazole-4-acetic acid, K and K' are N-methylarginine, and still further provided that when R^5 is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:



provided that $g+h+g'+k+h'+g''+h''+g'''$ is other than 0;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_s, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰; R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ and R^{9a} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁-C₅ alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁-C₅ alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_h;

R¹⁰ is independently selected at each occurrence from the group: a bond to C_h, COOR¹¹, OH, NHR¹¹, SO₃H, PO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, and a bond to C_h;

R¹² is a bond to C_h;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h'' is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

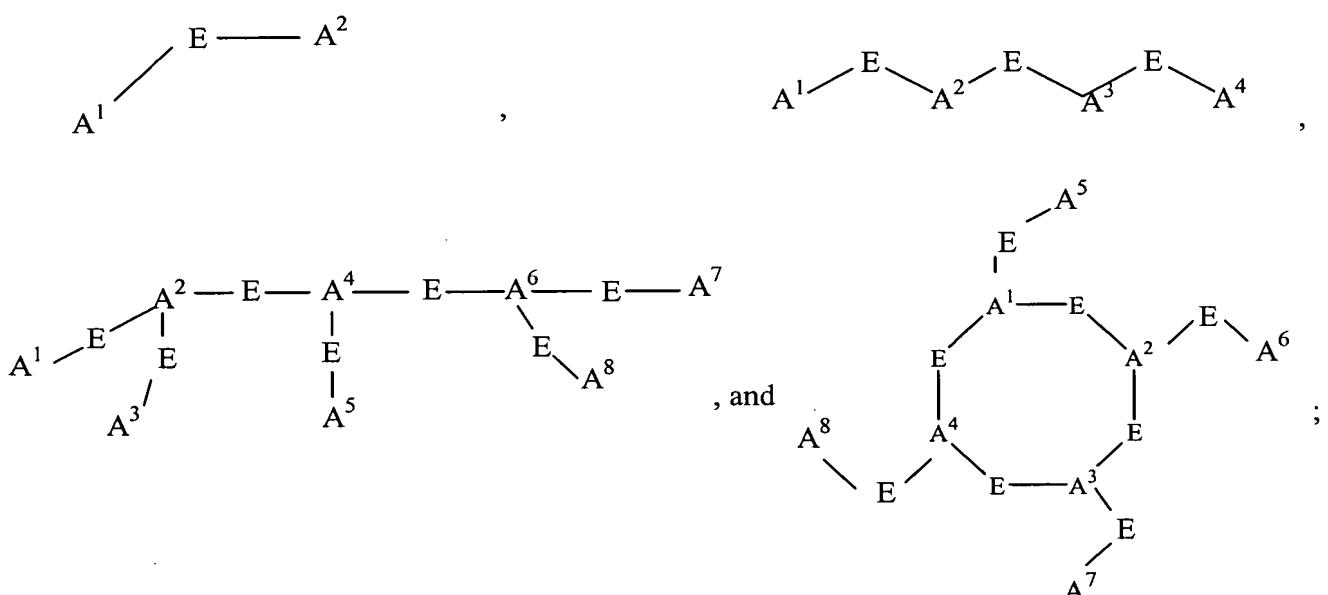
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

C_h is a metal bonding unit having a formula selected from the group:



$A^1, A^2, A^3, A^4, A^5, A^6, A^7$, and A^8 are independently selected at each occurrence from

the group $N, NR^{13}, NR^{13}R^{14}, S, SH, S(Pg), O, OH, PR^{13}, PR^{13}R^{14}, P(O)R^{15}R^{16}$, and a

bond to L_n ;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group:

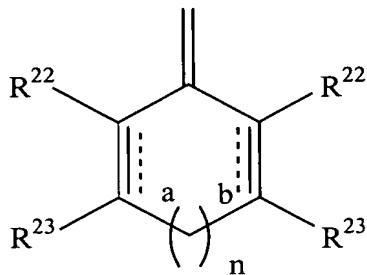
C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl C₆₋₁₀ aryl substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹³, and R¹⁴ are each independently selected from the group: a bond to L_n, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₁₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl C₆₋₁₀ aryl substituted with 0-3 R¹⁷, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³ or R¹⁴ is an electron, then the other is also an electron;

alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁵ and R¹⁶ are each independently selected from the group: a bond to L_n, OH, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl C₆₋₁₀ aryl substituted with 0-3 R¹⁷,

and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷; R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸, -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR^{19C}(=O)R¹⁸, -NR^{19C}(=O)OR^{18a}, -NR^{19C}(=O)N(R¹⁸)₂, -NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸, -S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸, NO₂, -C(=O)NHOR¹⁸, -C(=O)NHNR^{18a}R^{18a}, -OCH₂CO₂H, 2-(1 morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; R¹⁸, R^{18a}, and R¹⁹ are independently selected at each occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl; Pg is a thiol protecting group; R²⁰ and R²¹ are independently selected from the group: H, C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and unsaturated C₃₋₁₀ carbocycle substituted with 0-3 R²³; alternatively, R²⁰ and R²¹, taken together with the divalent carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24} , C_1 - C_{10} alkyl substituted with 0-3 R^{24} , C_2 - C_{10} alkenyl substituted with 0-3 R^{24} , C_2 - C_{10} alkynyl substituted with 0-3 R^{24} , aryl substituted with 0-3 R^{24} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{24} , and C_{3-10} carbocycle substituted with 0-3 R^{24} ;

alternatively, R^{22} , R^{23} taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R^{24} is independently selected at each occurrence from the group: =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, -N(R²⁵)₃+, -CH₂OR²⁵, -OC(=O)R²⁵, -OC(=O)OR^{25a}, -OR²⁵, -OC(=O)N(R²⁵)₂, -NR²⁶C(=O)R²⁵, -NR²⁶C(=O)OR^{25a}, -NR²⁶C(=O)N(R²⁵)₂, -NR²⁶SO₂N(R²⁵)₂, -NR²⁶SO₂R^{25a}, -SO₃H, -SO₂R^{25a}, -SR²⁵, -S(=O)R^{25a}, -SO₂N(R²⁵)₂, -N(R²⁵)₂, =NOR²⁵, -C(=O)NHOR²⁵, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy; and,

R^{25} , R^{25a} , and R^{26} are each independently selected at each occurrence from the group:

hydrogen and C_1 - C_6 alkyl;

and a pharmaceutically acceptable salt thereof.

4. (Rejected and On Appeal) A compound according to Claim 3, wherein:

L is glycine;

R¹ is an amino acid, optionally substituted with a bond to L_n, independently selected at each occurrence from the group: L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, phenylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, lysine, ornithine, 1,2-diaminobutyric acid, and 1,2-diaminopropionic acid;

R² is an amino acid, optionally substituted with a bond to L_n, independently selected at each occurrence from the group: valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

R³ is an amino acid, optionally substituted with a bond to L_n, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, and D-1,2-diaminopropionic acid;

R⁴ is an amino acid, optionally substituted with a bond to L_n, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-ornithine, D1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, and 2-aminothiazole4-acetic acid;

R⁵ is an amino acid, optionally substituted with a bond to L_n, independently selected at each occurrence from the group: L-valine, L-alanine, L-leucine, L-isoleucine, L-

norleucine, L-2-aminobutyric acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

d is selected from 1, 2, and 3;

W is independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_s, (OCH₂CH₂CH₂)_s, and (CH₂CH₂CH₂O)_t,

Z is selected from the group: aryl substituted with 0-1 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, C₁-C₅ alkyl substituted with 0-1 R¹⁰, aryl substituted with 0-1 R¹⁰, benzyl substituted with 0-1 R¹⁰, and C₁-C₅ alkoxy substituted with 0-1 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_h;

R¹⁰ is independently selected at each occurrence from the group: COOR¹¹, OH, NHR¹¹, SO₃H, aryl substituted with 0-1 R¹¹, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹¹, C₁-C₅ alkyl substituted with 0-1 R¹², C₁-C₅ alkoxy substituted with 0-1 R¹², and a bond to C_h;

R¹¹ is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², polyalkylene

glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin

substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², and a bond to C_h;

k is 0 or 1;

h is 0 or 1;

h' is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the

group: NR¹³, NR¹³R¹⁴, S, SH, S(Pg), OH, and a bond to L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group:

C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl

substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-

4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹³, and R¹⁴ are each independently selected from the group: a bond to L_n, hydrogen, C₁-C₁₀

alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, a 5-10 membered

heterocyclic ring system containing 1-4 heteroatoms independently selected from N,

S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³

or R¹⁴ is an electron, then the other is also an electron;

alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br,

I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CH₂OR¹⁸, -OC(=O)R¹⁸,

-OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a},

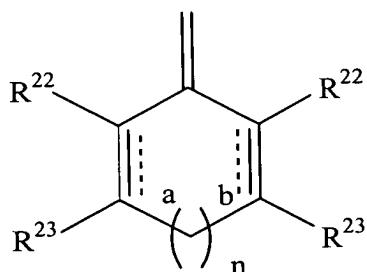
-NR¹⁹C(=O)N(R¹⁸)₂, -NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸, -C(=O)NHNR¹⁸R^{18a}, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy;

R₁₈, R_{18a}, and R₁₉ are independently selected at each occurrence from the group: a bond to

L_n, H, and C₁-C₆ alkyl;

R²⁰ and R²¹ are independently selected from the group: H, C₁-C₅ alkyl, -CO₂R²⁵, C₂-C₅ 1-alkene substituted with 0-3 R²³, C₂-C₅ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, and unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

alternatively, R²⁰ and R²¹, taken together with the divalent carbon radical to which they are attached form:



R²² and R²³ are independently selected from the group: H, and R²⁴;

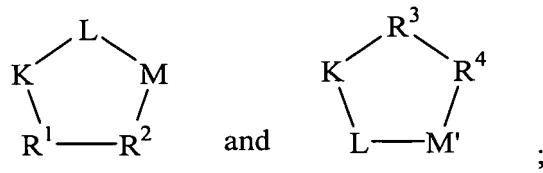
alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R²⁴ is independently selected at each occurrence from the group: -CO₂R²⁵, -C(=O)N(R²⁵)₂, -CH₂OR²⁵, -OC(=O)R²⁵, -OR²⁵, -SO₃H, -N(R²⁵)₂, and -OCH₂CO₂H; and,

R²⁵ is independently selected at each occurrence from the group: H and C₁-C₃ alkyl.

5. (Rejected and On Appeal) A compound according to Claim 4, wherein:

Q is a peptide selected from the group:



R¹ is L-valine, D-valine, D-lysine optionally substituted on the ε amino group with a bond to

L_n or L-lysine optionally substituted on the ε amino group with a bond to L_n;

R² is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid,

L-lysine optionally substituted on the ε amino group with a bond to L_n or tyrosine, the

tyrosine optionally substituted on the hydroxy group with a bond to L_n;

R³ is D-valine, D-phenylalanine, or L-lysine optionally substituted on the ε amino group with
a bond to L_n;

R⁴ is D-phenylalanine, D-tyrosine substituted on the hydroxy group with a bond to L_n, or L-
lysine optionally substituted on the ε amino group with a bond to L_n;

provided that one of R¹ and R² in each Q is substituted with a bond to L_n, and further

provided that when R² is 2-aminothiazole-4-acetic acid, K is N methylarginine;

d is 1 or 2;

W is independently selected at each occurrence from the group: NHC(=O), C(=O)NH,

C(=O), (CH₂CH₂O)_s, and (CH₂CH₂CH₂O)_t;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are independently selected at each occurrence from the
group: H, NHC(=O)R¹¹, and a bond to C_h;

k is 0;

h" is selected from 0, 1, 2, and 3;

g is selected from 0, 1, 2, 3, 4, and 5;

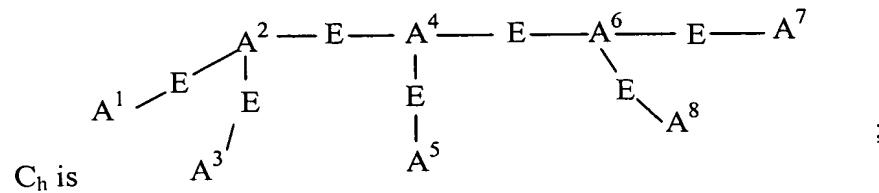
g' is selected from 0, 1, 2, 3, 4, and 5;

g'' is selected from 0, 1, 2, 3, 4, and 5;

g''' is selected from 0, 1, 2, 3, 4, and 5;

s' is 1 or 2;

t is 1 or 2;



A^1 is selected from the group: OH, and a bond to L_n ;

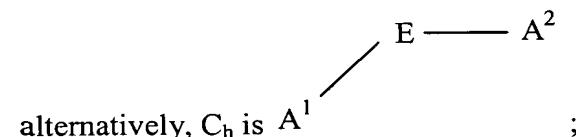
A^2 , A^4 , and A^6 are each N;

A^3 , A^5 , and A^8 are each OH;

A^7 is a bond to L_n or NH-bond to L_n ;

E is a C_2 alkyl substituted with 0-1 R^{17} ;

R^{17} is =O;



A^1 is NH_2 or $N=C(R^{20})(R^{21})$;

E is a bond;

A^2 is NHR^{13} ;

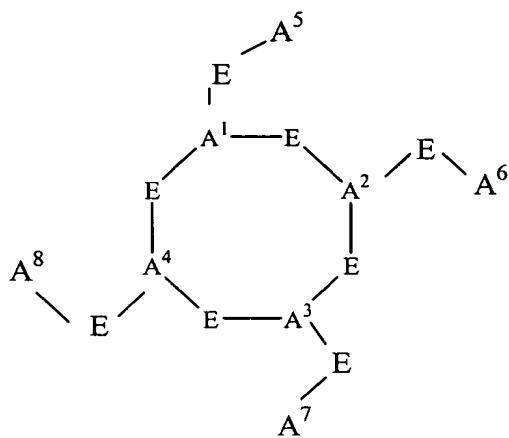
R^{13} is a heterocycle substituted with R^{17} , the heterocycle being selected from pyridine and pyrimidine;

R^{17} is selected from a bond to L_n , $C(=O)NHR^{18}$, and $C(=O)R^{18}$;

R^{18} is a bond to L_n ;

R^{24} is selected from the group: CO_2R^{25} , OR^{25} , SO_3H , and $N(R^{25})_2$;

R^{25} is independently selected at each occurrence from the group: hydrogen and methyl;



alternatively, C_h is

; ;

A¹, A², A³, and A⁴ are each N;

A⁵, A⁶, and A⁸ are each OH;

A⁷ is a bond to L_n;

E is a C₂ alkyl substituted with 0-1 R¹⁷; and,

R¹⁷ is =O.

6. (Rejected and On Appeal) A compound according to Claim 3, selected from the group:

(a) cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};

(b) cyclo{Arg-Gly-Asp-D-Tyr((N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-18-amino-14-aza-4,7,10-oxy-15-oxo-octadecoyl)-3-aminopropyl)-Val};

(c) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp})-cyclo{D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp};

(d) cyclo(Arg-Gly-Asp-D-Tyr-Lys([2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid)});

(e) cyclo {Arg-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])};

(f) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe};

(g) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-Phe-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe};

(h) cyclo {Arg-Gly-Asp-D-Nal-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])};

(i) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-Glu(cyclo {Lys-Arg-Gly-Asp-D-Nal})-cyclo {Lys-Arg-Gly-Asp-D-Nal};

(j) cyclo {Arg-Gly-Asp-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])-D-Val} ;

(k) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-Glu(cyclo {Lys-D-Val-Arg-Gly-Asp})-cyclo {Lys-D-Val-Arg-Gly-Asp};

(l) {cyclo(Arg-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};

(m) cyclo {D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])-D-Phe-D-Asp-Gly-Arg};

(n) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid]-Glu(cyclo {D-Lys-D-Phe-D-Asp-Gly-Arg})-cyclo {D-Lys-D-Phe-D-Asp-Gly-Arg};

(o) cyclo {D-Phe-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])-D-Asp-Gly-Arg};

(p) cyclo {N-Me-Arg-Gly-Asp-ATA-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-benzenesulfonic acid])};

- (q) cyclo {Cit-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (r) 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe};
- (s) cyclo {Arg-Gly-Asp-D-Phe-Lys(DTPA)};
- (t) cyclo {Arg-Gly-Asp-D-Phe-Lys}2(DTPA);
- (u) Cyclo {Arg-Gly-Asp-D-Tyr(N-DTPA-3-aminopropyl)-Val};
- (v) cyclo {Orn(d-N-2-Imidazolinyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (w) cyclo {Lys-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (x) cyclo {Cys(2-aminoethyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (y) cyclo {HomoLys-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (z) cyclo {Orn(d-N-Benzylcarbamoyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (aa) cyclo {Dap(b-(2-benzimidazolylacetyl))-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (bb) cyclo {Orn(d-N-2-Imidazolinyl)-Gly-Asp-D-Phe-Lys(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (cc) cyclo {Orn(d-N-Benzylcarbamoyl)-Gly-Asp-D-Phe-Lys(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};

(dd) cyclo {Lys-D-Val-D-Tyr(N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
(ee) cyclo {Orn(d-N-Benzylcarbamoyl)-D-Val-D-Tyr(N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
and,
(ff) cyclo {Orn(d-N-2-Imidazolinyl)-D-Val-D-Tyr(N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
or a pharmaceutically acceptable salt form thereof.

7. (Rejected and On Appeal) A kit comprising a compound of Claim 3, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.
8. (Rejected and On Appeal) A kit according to Claim 7, wherein the kit further comprises one or more ancillary ligands and a reducing agent.
9. (Rejected and On Appeal) A kit according to Claim 8, wherein the ancillary ligands are tricine and TPPTS.
10. (Rejected and On Appeal) A kit according to Claim 9, wherein the reducing agent is tin(II).
12. (Rejected and On Appeal) A metallopharmaceutical comprising the compound of Claim 1, and a radioisotope selected from the group: ^{99m}Tc , ^{95}Tc , ^{111}In , ^{62}Cu , ^{64}Cu , ^{67}Ga , and

^{68}Ga , wherein the targeting moiety is a peptide or a mimetic thereof and the linking group is present between the targeting moiety and chelator.

13. (Rejected and On Appeal) A metallopharmaceutical according to Claim 12, wherein the targeting moiety is a cyclic pentapeptide.

14. (Rejected and On Appeal) A metallopharmaceutical according to Claim 13, wherein the radioisotope is $^{99\text{m}}\text{Tc}$ or ^{95}Tc , and the metallopharmaceutical further comprises a first ancillary ligand and a second ancillary ligand capable of stabilizing the metallopharmaceutical.

15. (Rejected and On Appeal) A metallopharmaceutical according to Claim 14, wherein the radioisotope is $^{99\text{m}}\text{Tc}$.

16. (Rejected and On Appeal) A metallopharmaceutical according to Claim 15, wherein the metallopharmaceutical is selected from the group:

$^{99\text{m}}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr}(\text{N}-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-\text{Val}))$;

$^{99\text{m}}\text{Tc}(\text{tricine})(\text{TPPMS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-\text{D-Asp-Gly}))$;

$^{99\text{m}}\text{Tc}(\text{tricine})(\text{TPPDS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-\text{D-Asp-Gly}))$;

$^{99\text{m}}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-\text{D-Asp-Gly}))$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Phe-Lys(N-[5-[carbonyl]-2-pyridinyl]diazenido)}))$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr-Lys(N-[5-[carbonyl]-2-pyridinyl]diazenido}))$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})([2-[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-\text{benzenesulfonic acid]-Phe-Glu}(\text{cyclo}\{\text{Lys-Arg-Gly-Asp-D-Phe}\})-\text{cyclo}\{\text{Lys-Arg-Gly-Asp-D-Phe}\})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{Arg-Gly-Asp-D-Nal-Lys([2-[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-\text{benzenesulfonic acid}})\})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})([2-[[5-[carbonyl]-2-pyridinyl]-\text{hydrazone}]methyl]-\text{benzenesulfonic acid]-Glu}(\text{cyclo}\{\text{Lys-Arg-Gly-Asp-D-Nal}\})-\text{cyclo}\{\text{Lys-Arg-Gly-Asp-D-Nal}\})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr}((\text{N-[5-[carbonyl]-2-pyridinyl]diazenido}-18\text{-amino-14-aza-4,7,10-oxy-15-oxo-octadecoyl)-3-aminopropyl)-\text{Val}))$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{N-[5-[carbonyl]-2-pyridinyl]diazenido]-\text{Glu(O-cyclo(Lys-Arg-Gly-Asp-D-Phe))-O-cyclo(Lys-Arg-Gly-Asp-D-Phe))}$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{N-[5-[carbonyl]-2-pyridinyl]diazenido]-\text{Glu(O-cyclo(D-Tyr(3-aminopropyl)-\text{Val-Arg-Gly-Asp))-O-cyclo(D-Tyr(3-aminopropyl)-\text{Val-Arg-Gly-Asp}))})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-Lys(N-[5-[carbonyl]-2-pyridinyl]diazenido)})-\text{D-Val}))$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{D-Lys}([2-[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-\text{benzenesulfonic acid})-\text{D-Phe-D-Asp-Gly-Arg}\})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})([2-[[5-[carbonyl]-2-pyridinyl]hydrazone]methyl]-\text{benzenesulfonic acid]-Glu}(\text{cyclo}\{\text{D-Lys-D-Phe-D-Asp-Gly-Arg}\})-\text{cyclo}\{\text{D-Lys-D-Phe-D-Asp-Gly-Arg}\})$;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{D-Phe-D-Lys}([\text{2}-[[\text{5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-\text{benzenesulfonic acid}])-\text{D-Asp-Gly-Arg}\});$
 $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{N-Me-Arg-Gly-Asp-ATA-D-Lys}(\text{N}-[\text{5-[carbonyl]-2-pyridinyl]diazenido])))$);
 $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{Cit-Gly-Asp-D-Phe-Lys}([\text{2}-[[\text{5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-\text{benzenesulfonic acid}])\})$; and,
 $^{99m}\text{Tc}(\text{tricine})(1,2,4\text{-triazole})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr}(\text{N}-[\text{5-[carbonyl]-2-pyridinyl]diazenido]-3\text{-aminopropyl})-\text{Val}))$.

17. (Rejected and On Appeal) A metallopharmaceutical according to Claim 13, wherein the radioisotope is ^{111}In .

18. (Rejected and On Appeal) A metallopharmaceutical according to Claim 17, wherein the metallopharmaceutical is selected from the group:

(DOTA- ^{111}In)-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};
cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- ^{111}In)); and
cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA- ^{111}In).

19. (Rejected and On Appeal) A metallopharmaceutical comprising the compound of Claim 1 and a radioisotope selected from the group: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , ^{109}Pd , ^{159}Gd , ^{140}La , ^{198}Au , ^{199}Au , ^{169}Yb , ^{175}Yb , ^{165}Dy , ^{166}Dy , ^{67}Cu , ^{105}Rh , ^{111}Ag , and ^{192}Ir , the targeting moiety is a peptide or a mimetic thereof and the linking group is present between the targeting moiety and chelator.

20. (Rejected and On Appeal) A metallopharmaceutical according to Claim 19, wherein the targeting moiety is a cyclic pentapeptide.

21. (Rejected and On Appeal) A metallopharmaceutical according to Claim 20, wherein the radioisotope is ^{153}Sm .

22. (Rejected and On Appeal) A metallopharmaceutical according to Claim 21, wherein the metallopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- ^{153}Sm));
cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA- ^{153}Sm); and,
cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(^{153}Sm)-3-aminopropyl)-Val).

23. (Rejected and On Appeal) A metallopharmaceutical according to Claim 20, wherein the radioisotope is ^{177}Lu .

24. (Rejected and On Appeal) A metallopharmaceutical according to Claim 23, wherein the metallopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- ^{177}Lu));
(DOTA- ^{177}Lu)-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe};
cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA- ^{177}Lu); and
cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(^{177}Lu)-3-aminopropyl)-Val).

25. (Rejected and On Appeal) A metallopharmaceutical according to Claim 20, wherein the radioisotope is ^{90}Y .

26. (Rejected and On Appeal) A metallopharmaceutical according to Claim 25, wherein the metallopharmaceutical is:

(DOTA-⁹⁰Y)-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};

27. (Rejected and On Appeal) A metallopharmaceutical comprising the compound of Claim 1 and, a paramagnetic metal ion selected from the group: Gd(III), Dy(III), Fe(III), and Mn(II), wherein the targeting moiety is a peptide or a mimetic and the linking group is present between the targeting moiety and chelator.

28. (Rejected and On Appeal) A metallopharmaceutical according to Claim 27, wherein the targeting moiety is a cyclic pentapeptide.

29. (Rejected and On Appeal) A metallopharmaceutical according to Claim 28, wherein the metal ion is Gd(III).

30. (Rejected and On Appeal) A metallopharmaceutical according to Claim 29, wherein the contrast agent is:

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(Gd(III))-3-aminopropyl)-Val).

31. (Rejected and On Appeal) A metallopharmaceutical comprising the compound of Claim 1 and a metal selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, wherein the targeting moiety is a cyclic pentapeptide, and the linking group is present between the targeting moiety and chelator.

32. (Rejected and On Appeal) A method of treating rheumatoid arthritis in a patient comprising: administering a metallopharmaceutical of Claim 19 capable of localizing in Previously Presented² angiogenic vasculature to a patient by injection or infusion.

33. (Rejected and On Appeal) A method of treating cancer in a patient comprising: administering to a patient in need thereof a metallopharmaceutical of Claim 19 by injection or infusion.

34. (Rejected and On Appeal) A method of imaging formation of new blood vessels in a patient comprising: (1) administering a metallopharmaceutical comprising the compound of Claim 1 and a metal to a patient by injection or infusion; (2) imaging the area of the patient wherein the desired formation of Previously Presented² blood vessels is located.

35. (Rejected and On Appeal) A method of imaging cancer in a patient comprising: (1) administering a metallopharmaceutical of Claim 12 to a patient by injection or infusion; (2) imaging the patient using planar or SPECT gamma scintigraphy, or positron emission tomography.

² The response of Feb. 18, 2005, erroneously recited "Previously Presented" in place of "new" through a clerical error involving MS Word's "find and replace" feature. No amendment was intended. Appellants admit the error, but are concerned that restoring the word "new" now might be taken as an amendment in contravention of 37 CFR 41.37(c)(2). Thus, Appellants plan to correct it at the first opportunity.

48. (Rejected and On Appeal) A therapeutic radiopharmaceutical composition, comprising:

- (a) a metallopharmaceutical of Claim 19; and,
- (b) a parenterally acceptable carrier.

49. (Rejected and On Appeal) A diagnostic radiopharmaceutical composition, comprising:

- (a) a metallopharmaceutical comprising the compound of Claim 1 and a metal; and,
- (b) a parenterally acceptable carrier.

50. (Rejected and On Appeal) A therapeutic radiopharmaceutical composition, comprising:

a radiolabelled targeting moiety, wherein the targeting moiety is a compound Q of
Claim 3 and the radiolabel is a therapeutic isotope selected from the group: ^{35}S , ^{32}P ,
 ^{125}I , ^{131}I , and ^{211}At .

52. (Rejected and On Appeal) A compound comprising a peptide or peptidomimetic α,β_3
receptor targeting moiety bound to a chelator.

53. (Rejected and On Appeal) A compound, comprising a peptide or peptidomimetic α,β_3
receptor targeting moiety bound to a chelator, wherein said chelator is a
diaminedithiol, monoamine-monoamidedithiol, triamide-monothiol, monoamine-
diamide-monothiol, diaminedioxime, hydrazine, or cyclic polyaminocarboxylate, or
acyclic polyaminocarboxylate.

9. EVIDENCE APPENDIX

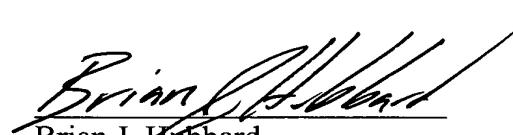
None.

10. RELATED PROCEEDINGS APPENDIX

None.

Date:

Jan 25, 2006



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